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10/594,962	09/29/2006	Tomoki Todo	042715-5023	6716

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EXAMINER	
HAMA, JOANNE	

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,962	TODO ET AL.	
	Examiner	Art Unit	
	JOANNE HAMA	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 16-20* is/are pending in the application.

4a) Of the above claim(s) *12-14, 16-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's species election without traverse of "IL-12" (as recited in claim 11) in the reply filed on April 7, 2009 is acknowledged.

Claims 12-14, 16-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 7, 2009.

Applicant is reminded that since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits, see Restriction, March 2, 2009. Accordingly, claims 17-20 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Applicant is reminded that all claims in amendments be given the proper status identifier or risk non-entry of amendments (see 37 CFR 1.121). It is noted that the status of claims 17-20 is "withdrawn."

Claim 15 is cancelled.

Claims 1-11, drawn to a method for constructing recombinant herpes simplex virus, are under consideration.

Applicant filed a response to the Non-Final Action of July 28, 2008, on November 25, 2008. It is noted that Applicant has also included amendments to the claims November 25, 2008, December 12, 2008, December 15, 2008.

Applicant indicates that if the Examiner believed that claims 5-20 were in improper dependent form, the Examiner should have objected to these claims, rather than withdraw these claims. See MPEP §608.01(n)(II), Applicants respectfully request that the Examiner remove any objection to currently amended claims 5-20 and place them under consideration for substantive examination (Applicant's response, page 6). In response, with regard to Applicant indicating that claims 5-20 should have been objected to, MPEP § 608.01(n)(II) refers to claims being of improper dependent for failing to further limit the subject matter of a previous claim. This was not the case of the instant claims. Rather, the situation for the instant claims was that the claims were in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim (MPEP 608.01(n)). As such, claims 5-20 were not further treated on the merits, and the Examiner's withdrawal of the claims was appropriate.

Withdrawn Objection

Claim Objection

Applicant's arguments, see page 6 of Applicant's response, filed November 25, 2008, with respect to the objection of claims 1-4 have been fully considered and are persuasive. Applicant indicates that "FRP site" has been amended to "FRT site." The objection of claims 1-4 has been withdrawn.

New/Maintained Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 remain rejected in modified form and amended claims 5-9 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Chiocca et al., US Patent Application Publication US 2002/0110543 A1, published August 15, 2002, previously cited, in view of Breakefield et al., US Patent, 6,573,090, patented June 3, 2003, Saeki et al., 2001, Molecular Therapy, 3: 591-60, Buchholz et al., 2001, Nature Biotechnology, 19: 1047-1052, previously cited, Krisky et al., 1998, Gene Therapy, 5: 1517-1530, previously cited, Todo et al., 2001, Cancer Research 61: 153-161, Bennett et al., 2001, Annals of Surgery, 233: 819-826, for reasons of record July 28, 2008.

Applicant's amendments raise new grounds of rejection, which are as follows. Response to Applicant's rebuttals, filed November 25, 2008 follows the new grounds of rejection.

As indicated in the Office Action, July 28, 2008, Chiocca et al. teach a BAC clone comprising the genomic sequence of Herpes Simplex Virus I (HSV-I, about 160kb) and a transgene-transfer plasmid (pTransfer, 2kb). Chiocca et al. teach that the pTransfer construct comprising genes of interest is inserted into the BAC clone and following

recombination that removed the prokaryotic backbone in the BAC clone, a construct comprising the viral genome and the transgenes of interest was made and oncolytic virus was made following expression of the construct (Chiocca et al., Example 2).

While Ciocca et al. teach a transfer plasmid comprising transgenes of interest, Chiocca et al. do not specifically teach that the transfer plasmid comprises "stuffer" sequence (see claim 1, step 2).

With regard to claim 1 being drawn the shuttle vector containing a stuffer sequence and that following the integration of the shuttle vector into the herpes simplex virus genome, the entire BAC-shuttle vector construct is about 168k nucleotides or larger after insertion of the shuttle vector or is 170k nucleotides or larger after the insertion of the shuttle vector, including the nucleotides encoding the target protein, Breakefield et al. teach that BAC clones that comprise DNA that is more than 150 kb in length cannot package the DNA into viral capsids, as the size of the DNA exceeds what can fit into a viral capsid. The advantage of this is that the inability to close capsids reduces helper-virus contamination (Breakefield et al., col. 5, 5th parag. to col. 6, 3rd parag.). One example of a shuttle vector comprising stuffer DNA is ploxP-K ICP0, taught by Saeki et al. Saeki et al. teach that ploxP-K ICP0, inserted into the BAC clone comprising the HSV-1 genome results in a 178kb construct (Saeki et al., abstract). It is noted that with regard to the claims being drawn to the BAC-shuttle vector comprising a transgene of interest (e.g. CMV promoter and a nucleic acid encoding IL-12), the art teaches that the CMV promoter and IL-12 sequences were known at the time of filing (e.g. see Todo et al. and Bennett et al.).

With regard to the claims being drawn to marker genes that are inserted into the BAC plasmid or into the shuttle vector (claims 5, 8, 9), Chiocca et al. teach drug resistance markers and fluorescent markers are used to monitor transgene constructs (Chiocca et al., Example 2 and Figure 7). For example, the BAC clone has a chloramphenicol-resistance gene and the pTransfer vector has an ampicillin resistance gene (Chiocca et al., parag. 186, Figure 7). The BAC clone also has a gene encoding a red fluorescent protein (RFP) and a GFP fusion protein construct. Following integration of the pTransfer vector into the BAC clone, cells are treated with a recombinase to remove part of the prokaryotic backbone of the BAC clone, the viral genome containing the gene of interest was released. Clones that were positive for GFP and negative for RFP was indicative that recombination was successful.

With regard to the claims being drawn to a promoter contained in at least one type of expression cassette of a gene encoding the target protein (claims 5-7, 10, 11), Chiocca et al. teach a transgene cassette of interest (x) is cloned into the MCS of pTransfer. The transgene cassette of interest can comprise a number of different therapeutic proteins (Chiocca et al., parag. 114-117). With regard to this vector having applications in cancer (note that Chiocca et al. teach that HSV-1 is an oncolytic virus that can be used in cancer therapy, Chiocca et al., parag. 187), Chiocca et al. teach that the transgene can include immune enhancers (Chiocca et al., parag. 116). At the time of filing, the art teaches that the CMV promoter can be used to drive expression of an immunomodulatory gene used in tumor treatment (Todo et al., abstract). While Todo et al. teach the use of B7, the art teaches that IL-12 was used with an oncolytic HSV to

lyse tumor cells and to provide the host immune system with the cytokine stimulus necessary to recruit and activate inflammatory cells needed to enhance the antitumor effect (Bennett et al., page 819, under Summary Background Data). As such, an artisan would have used a construct comprising a nucleic acid sequence encoding IL-12 operably linked to a CMV promoter. An artisan would have done so because the CMV promoter works in the oncolytic herpes virus system and IL-12 is used by artisans to induce an immune response against tumors.

Applicant's arguments filed November 25, 2008 have been fully considered but they are not persuasive.

Applicant indicates that claim 1 has been amended to specify that the shuttle vector comprises stuffer sequence (Applicant's response, page 7). In response, the Examiner has addressed the issue that the shuttle vector has stuffer sequence (see Breakefield et al. and Saeki et al.).

Applicant indicates that Chiocca does not teach or suggest the use of the HSV genome having a suitable length for identifying the virus containing the target recombinant HSV genome in light with the mechanism of the production of the HSV virus (Applicant's response, page 8). In response, with regard to length, Breakefield et al. and Saeki et al. teach capsids cannot be stuffed with DNA of a certain length and that the advantage of using vectors that are larger than what the capsid can hold is that the packaging system is helper virus-free.

Applicant indicates that neither Buchholz nor Krisky teach the use of stuffer sequence (Applicant's response, page 8). In response, the Examiner relied on Breakefield et al. and Saeki et al.

Thus, the claims remain rejected.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-

272-2911. The examiner can normally be reached Mondays, Tuesdays, Thursdays, and Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/Joanne Hama/
Primary Examiner
Art Unit 1632